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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,124	07/18/2003	Martin F. Bachmann	1700.0340001/BJD/SJE	3313

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STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
BOESEN, AGNIESZKA	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 07/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/622,124	BACHMANN ET AL.	
	Examiner	Art Unit	
	Agnieszka Boesen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,19,22-25,27-34,55 and 61-90* is/are pending in the application.

4a) Of the above claim(s) *5,9,10,30,41,49,50,54,56-62,67,71,74 and 90* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/27/04 and 9/29/0*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims rejected are 1-4, 6-8, 11-15, 19, 21-29, 31-34, 55, 63-66, 68-70, 72, 73, and 75-89.

DETAILED ACTION

The Amendment filed May 4, 2006 in response to the Office Action of January 12, 2006 is acknowledged and entered. Claims 63-90 have been added. Claims 1-15, 19, 22-25, 27-34, 55, 61-90 are pending. Claims 5, 9, 10, 30, 41, 49, 50, 54, 56-62, 67, 71, 74, and 90 are withdrawn. Claims 1-4, 6-8, 11-15, 19, 21-29, 31-34, 55, 63-66, 68-70, 72, 73, 75-89 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

The Examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Agnieszka Boesen Group Art Unit 1648.

Election/Restriction

Applicant's election of species of SEQ ID NO: 4, which is the amino acid sequence of the coat proteins of RNA bacteriophage, and SEQ ID NO: 65, which is the sequence of the second attachment site of the core particle, in response to the restriction requirement on January 12, 2006 is acknowledged.

The amended claims 61 and 62 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claim 61, as originally presented was directed to a composition of claim 1 for use as a medicament, classified in class

424, subclass 94.1. Claim 61, as currently amended is directed to a method of treating a disorder or disease in an animal, classified in class 435, subclass 69.3.

Claim 62, as originally presented was directed to a use of a composition of claim 1 for the manufacture of a medicament for treatment of obesity, classified in class 435, subclass 69.3. Claim 62, as currently amended is directed to a different method of treating obesity in an animal, classified in class 435, subclass 330. The elected product claims and the methods of using (claims 61 and 62) are distinct because the product as claimed can be used in another materially different method of use such as in the method of detection of flaviviruses.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 61 and 62 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 101

The rejection of claim 20 under 35 U.S.C. 101 is moot because the Applicant has canceled claim 20.

Applicant's arguments, see Remarks page 24 and 25, have been fully considered and are persuasive. Therefore, the rejection of claims 1-3, 19, 22-29 under 35 U.S.C. 101 for reading on a product of nature **is withdrawn.**

Claim Rejections - 35 USC § 112

The rejection of claims 16-18, 20, and 35-54 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention is moot because the Applicant has canceled claims 16-18, 20, and 35-54.

Applicant's arguments, see Remarks page 25-29, have been fully considered and are persuasive. Therefore, the rejection of claims 1-4, 6-8, 11, 13-15, 19, 21-29, 31-34, 55, 61, and 62 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "naturally occurring" and "mutant coat proteins" **is withdrawn.**

The rejection of claims 28 and 29 under 35 U.S.C. 112, second paragraph, for lacking antecedent basis for "said amino acid linker" **is withdrawn** in view of Applicants amendments to the claims.

Applicant's arguments, see Remarks page 30-34, have been fully considered and are persuasive. Therefore, the rejection of claims 1-4, 6-8, 11, 13-15, 19, 21-29, 31-34, 55, 61 and 62 under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement **is withdrawn.**

Claim Rejections - 35 USC § 102

Applicant's arguments, see Remarks page 34, with respect to the rejection(s) of claim(s) 1-3, 19, 20, 22-29 and 31 under 35 U.S.C. 102(b) have been fully considered and are persuasive. Therefore, the rejection **is withdrawn.**

Claim Rejections - 35 USC § 103

The rejection of claims 35-40, 42, 43, 48, and 51-53 under 35 U.S.C. 103(a) is moot because the Applicant has canceled claims 35-40, 42, 43, 48, and 51-53.

Applicant's arguments, see Remarks page 37, with respect to the rejection(s) of claim(s) 4, 6-8, 11, 13, 14, 21, 32-34, 55, 61 and 62 under 35 U.S.C. 103(a) have been fully considered and are persuasive. Therefore, the rejection **is withdrawn**.

Applicant's arguments, see Remarks page 39, with respect to the rejection(s) of claim(s) 15-18 and 44-47 under 35 U.S.C. 103(a) have been fully considered and are persuasive. Therefore, the rejection **is withdrawn**. However, upon further consideration a new ground(s) of rejection is made in view of newly found prior art references.

New claim objections and rejections.

Claim Objections

Claim 61, is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1; claim 64 is a substantial duplicate of claim 2; claim 66 is a substantial duplicate of claim 4, claim 68 is a are substantial duplicate of claim 6; claim 69 is a substantial duplicate of claim 7; claim 70 is a substantial duplicate of claim 8; claim 71 is a substantial duplicate of claim 9-11; claims 72 and 72 are substantial duplicate of claim 12; claim 76 is a substantial duplicate of claim 15; claim 77 is a substantial duplicate of claim 19; claim 78 is a substantial duplicate of claim 22, claim 79 is a substantial duplicate of claim 23; claim 80 is a substantial duplicate of claim 25, claim 81 is a substantial duplicate of claim 27; claim 82 is a substantial duplicate of claim 28;

claim 83 is a substantial duplicate of claim 29; claim 84 is a substantial duplicate of claim 30; and claim 85 is a substantial duplicate of claim 31 . When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 15, 19, 21-31, 32-34, 55, 63, 64, and 76-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sebbel et al., (US Patent 6,964,769 B2, herein, "Sebbel") in view of Kojima et al (Nature, 1999, herein, "Kojima").

Claims are drawn to a composition comprising a core particle with at least one first attachment site and at least one antigen or antigenic determinant with at least one second attachment site, wherein the antigenic determinant such as ghrelin peptide and the core particle interact trough an association to form an ordered and repetitive antigen array. The first attachment site comprises an amino group and a second attachment site comprises a sulfhydryl group. The attachment site can be not-naturally occurring or naturally occurring. The antigenic determinant is a human ghrelin or a ghrelin peptide. The core particle is a bacteriophage. The

proteins of the RNA bacteriophage have been modified by removal, substitution or addition of a lysine residue. The second attachment site is associated with first attachment site through at least one covalent bond. The sequence of the ghrelin peptide is SEQ ID NO: 31 which is: GSSFLSPEHQRVQQRKESKKPPAKLQPR. The ghrelin peptide comprises an amino acid linker, which comprises second attachment site. The ghrelin peptide lacks an n-octanoyl modification. The composition comprises a pharmaceutically acceptable carrier and an adjuvant. The composition is devoid of an adjuvant. The core particle is a recombinant virus-like particle. The claims are also drawn to a process for producing the composition of current claim 1.

Applicant defined the first and second attachment site in the specification as:

The phrase "first attachment site" refers to an element of non-natural or natural origin, to which the second attachment site located on the antigen or antigenic determinant may associate. The first attachment site may be a protein, a polypeptide, an amino acid, a peptide, a sugar, a polynucleotide, a natural or synthetic polymer, a secondary metabolite or compound (biotin, fluorescein, retinol, digoxigenin, metal ions, phenylmethylsulfonylfluori- de), or a combination thereof, or a chemically reactive group thereof. The first attachment site is located, typically and preferably on the surface, of the core particle such as, preferably the virus-like particle. Multiple first attachment sites are present on the surface of the core and virus-like particle, respectively, typically in a repetitive configuration.

The phrase "second attachment site" refers to an element associated with the antigen or antigenic determinant to which the first attachment site located on the surface of the core particle and virus-like particle, respectively, may associate. The second attachment site of the antigen or antigenic determinant may be a protein, a polypeptide, a peptide, a sugar, a polynucleotide, a natural or synthetic polymer, a secondary metabolite or compound (biotin, fluorescein, retinol, digoxigenin, metal ions, phenylmethylsulfonylfluoride), or a combination thereof, or a chemically reactive group thereof. At least one second attachment site is present on the antigen or antigenic determinant. The term "antigen or antigenic determinant with at least one second attachment site" refers, therefore, to an antigen or antigenic construct comprising at least the antigen or antigenic determinant and the second attachment site. However, in particular for a second attachment site, which is of non-natural origin, i.e. not naturally occurring within the antigen or antigenic determinant, these antigen or antigenic constructs comprise an "amino acid linker".

Sebbel (US Patent 6,964,769 B1) teaches a composition comprising a core particle with at least one first attachment site and at least one antigen or antigenic determinant with at least one second attachment site wherein the antigenic determinant and the core particle interact through an association to form an ordered and repetitive antigen array (see the entire document, particularly claims 1-24, columns 5-7, columns 10, 15, 16). The core particle taught by Sebbel is a virus, a virus-like particle, a bacterial pilus, a structure formed from bacterial pilin, a bacteriophage, a viral capsid particle or a recombinant form thereof. Sebbels' first and second attachment site of the core particle, as they are defined, are exactly the same (see column 10, lines 33-58) as the first and second attachment sites currently claimed. The attachment site taught by Sebbel is either naturally occurring or non-naturally occurring (see column 14, lines 38-45). Sebbel teaches the second attachment site associated with first attachment site through at least one covalent bond (see column 12, line 15-20). Sebbel teach the first attachment site comprising an amino group and a second attachment site comprising a sulfhydryl group (see claim 3). Sebbel teach a linker connecting the peptide of interest to the core particle (see Example 19). Sebbel teach modification of the core particle residues by removal, addition, or substitution of lysine residues. Sebbel further teach that the elimination of these lysine residues results in the removal of binding sites for antigens or antigenic determinants which could disrupt the ordered array and should improve the quality and uniformity of the final vaccine composition (see column 24, lines 51-61).

It is noted that the person of ordinary skill in the art would provide a ghrelin peptide that lacks an n-octanoyl modification for the purpose of making a construct of a core particle and an antigenic determinant. Kojima teach that ghrelin peptide purified from human stomach extract

has an n-octanoyl modification (see page 658, second paragraph on the left column). The person of ordinary skill in the art would not include the n-octanoyl modification in the synthetically made ghrelin peptide because such modification is not necessary for the peptide to be immunogenic which is the purpose of the current invention.

The composition taught by Sebbel comprises a pharmaceutically acceptable carrier and an adjuvant (see claims 9 and 11). Sebbel teaches the pharmaceutical composition without an adjuvant (see column 3, lines 42-48). Sebbel teach a process for producing the composition comprising a core particle and the antigenic determinant (see claim 18).

Although Sebbel teaches that any antigen of choice could be coupled to the surface of a virus like particle or a bacteriophage (see column 6, lines 21-38), Sebbel does not expressly teach ghrelin antigen or ghrelin peptide.

Kojima et al. teach a human ghrelin peptide, which has the sequence identical to the sequence of the instantly claimed SEQ ID NO: 31 (see page 658, Figure 4, ghrelin sequence is boxed). The ghrelin peptide of SEQ ID NO: 65, with the second attachment site, is exactly the same peptide as SEQ ID NO: 31 except that peptide of SEQ ID NO: 65 has an additional cysteine residue on the amino terminus. It is herein interpreted that the cysteine residue on the C terminal of the ghrelin peptide serves as the attachment site. Sebbel teach a cysteine residue as useful amino acid comprised within the second attachment site for the purpose of linking the antigenic determinant to the core particle (see column 5, lines 11-16).

It would have been obvious for the person of ordinary skill in the art to provide Sebbels' pharmaceutical composition comprising an antigenic determinant such as ghrelin or a ghrelin peptide taught by Kojima, because Sebbel teach that any antigen of choice could be coupled to

the surface of a virus like particle or a bacteriophage. One would have been motivated to couple ghrelin or a ghrelin peptide taught by Kojima to the surface of a virus like particle or a bacteriophage because Sebbel teaches that coupling an antigen of interest to the core particle such as for example a becatriophage, provides compositions suited for the efficient induction of desired immune responses. One would have had a reasonable expectation of success to make a Sebbels' composition comprising Kojimas' ghrelin peptide because because such constructs are routinely made in the art using methods of recombinant DNA technology. Therefore, at the time of the instant invention, the claims would have been obvious over Sebbels' composition and Kojimas' peptide.

Claims 4, 6-8, 11-14, 31, 66, 68-70, 72, 73, 75, and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sebbel et al., (US Patent 6,964,769 B2, herein, "Sebbel") in view of Kojima et al (Nature, 1999, herein, "Kojima") as applied to claims 1-3, 19, 21-30, 32-34, 55, 63, 64, and 77-84 above, and further in view of Vasiljeva et al. (FEBS Letters, 1998) and Maita et al. (Gen Pept Accession VCBPQB, 1971).

Claims are drawn to a composition wherein the core particle such as a virus like particle comprises recombinant proteins of RNA Qβ-bacteriophage having an amino acid sequence of SEQ ID NO: 4.

Sebbel and Kojima teach a composition comprising a core particle and the antigenic determinant such as ghrelin peptide as noted above. However, Sebbel and Kojima do not teach Qβ-bacteriophage having an amino acid sequence of SEQ ID NO: 4.

Vasiljeva teach using recombinant RNA Qβ-bacteriophage as a carrier for the administration of antigenic peptides. Maita teach coat protein of Qβ-bacteriophage, which sequence is identical to the currently claimed SEQ ID NO: 4.

It would have been obvious to the person of ordinary skill in the art to use recombinant RNA Qβ-bacteriophage core protein of SEQ ID NO: 4 as a core particle and a carrier for the administration of antigenic peptides such as ghrelin peptide. One would have been motivated to provide Sebbels' composition comprising RNA Qβ-bacteriophage core protein of SEQ ID NO: 4 taught by Vasiljeva and Maita and the antigenic determinant such as ghrelin peptide taught by Kojima, because Vasiljeva teach that recombinant RNA Qβ-bacteriophage particles are effective for induction of desired immune responses to the encoded antigenic determinants.

One would have had a reasonable expectation of success to make a construct of RNA Qβ-bacteriophage core protein and ghrelin peptide because such constructs are routinely made in the art using methods of recombinant DNA technology as taught by Sebbel and Vasiljeva. Therefore, at the time of the instant invention, the claims would have been obvious over Sebbels composition, Kojimas' peptide, Vasiljevas' Qβ-bacteriophage and Maitas' sequence.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnieszka Boesen whose telephone number is 571-272-8035. The examiner can normally be reached on 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AB

Agnieszka Boesen, Ph.D.
Examiner

7/14/06

Stacy B. Chen 7/17/06

STACY B. CHEN
PRIMARY EXAMINER